REMARKS

Claims 47-107 were previously submitted for examination. Claims 47-68 and 98-107 were withdrawn from consideration. Claims 1-46 were canceled by the Preliminary Amendment submitted on January 16, 2004 and claims 72-77, 85, 87-91 and 94 were canceled by the March 23, 2007 Amendment. Claims 70, 82, 108-112, 114-119, 121-126 and 128-131 have been cancelled, 69, 78, 79, 86 and 92 have been amended, and new claims 132-147 have been added by the present Amendment. Therefore claims 69, 71, 78-81, 83, 84, 86, 92, 93, 95-97, 113, 120, 127 and 132-147 are under active consideration.

Support for the amended claims 69, 78 and 92 for reciting an "isolated antibody that specifically binds to a three-dimensional epitope of a parathyroid hormone (PTH) in PTH_{1-8} as part of whole PTH, wherein ~~s~~ at least four amino acids in PTH_{1-8} are part of the reactive portion of said isolated antibody," and support for the amended claim 86 for reciting an "said polyclonal antibody specifically binds to said three-dimensional epitope in human PTH_{1-8} as part of whole human PTH, at least four amino acids in PTH_{1-8} are part of the reactive portion of said isolated polyclonal antibody" can be found throughout the present application as originally filed, and *inter alia* at page 5, line 25 through page 6, line 1, at page 11, lines 7-13, and at page 12, lines 8-12; *see also* the parent application, U.S. patent application Serial No. 09/344,639 ('639 application) at page 5, line 24 through page 6, line 1, at page 11, lines 7-13, and at page 12, lines 8-12; U.S. patent application Serial No. 08/231,422 ('422 application) at page 7, line 26 through page 8, line 2; and page 8, lines 24-28.

Support for the amended claims 69, 78 and 92 for reciting an "said isolated antibody does not specifically bind to a non-(1-84) PTH fragment," and support for the amended claim 86 for reciting an "said isolated polyclonal antibody does not specifically bind to a non-(1-84) PTH fragment" can be found throughout the present application as originally filed, and *inter alia* at page 5, lines 12-25; *see also* the '639 application at page 5, lines 11-24; and the '422 application at page 3, lines 28-29.

Support for the new claims 132-147 for reciting an at least five, six, seven and eight amino acids in PTH_{1-8} are part of the reactive portion of the isolated antibody, respectively, an be found throughout the present application as originally filed, and *inter alia* at page 5, line 25 through page 6, line 1; *see also* the '639 application at line 24 through page 6, line 1.

Accordingly, the present amendments do not introduce any new matter. Entry of the amendments is respectfully requested.

With respect to all amendments and canceled claims, applicants have not dedicated or abandoned any unclaimed subject matter and moreover have not acquiesced to any rejections and/or objections made by the Patent Office. Applicants reserve the right to pursue prosecution of any presently excluded claim embodiments in future continuation and/or divisional applications.

Priority

Regarding the priority claim, the Examiner states:

> It is noted that Applicant argues the priority of instant case is based on its parent cases, i.e. US 09344039 (now US Patent 6743590) and US 09231422 (now US Patent 6689566). However, due to lack of support from the specification, the current application is accorded priority date based on its filing date, i.e. 1/16/2004 (See below New Matter Rejection)(Also see below). (The Final Office Action at page 2.)

Applicants respectfully submit that the presently pending claims are entitled to the filing dates to the parent applications, the '639 application and/or the '422 application, for the reasons discussed below as a response to the written description (new matter) rejection.

Rejection under 35 U.S.C. § 112, first paragraph - New matter

The rejections of claims 69, 71, 78-84, 86, 92-93, 95-97 and 108-131 under 35 U.S.C. 112, first paragraph, as allegedly failing to comply with the written description requirement are maintained. The Examiner alleged that the claims contain subject matter which was not described

in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. According to the Examiner:

> It is noted that the instant claims 69, 78, 92 and 86 recite "an antibody binds to a bioactive epitope of a parathyroid hormone (PTH) in PTH_{1-8} or PTH_{1-9} wherein said isolated antibody binds to said epitope within a whole PTH with a higher affinity than its binding to said epitope within a PTH fragment selected from a PTH_{1-8} fragment, PTH_{1-9}, PTH_{1-10} and PTH_{1-34} fragment".
>
> It is also noted that PTH_{1-9} and PTH_{1-10} are new matters not supported by specification.
>
> The original specification amendment filed on 1/16/2004, at page 11, line 7, Applicant requested to enter SEQ ID No. 4 (human PTH_{1-8} fragment) and SEQ ID No. 7 (rat PTH_{1-8} fragment), where both the sequence has only **8** amino acid which spans from 1-8 of the PTH molecule (emphasis added).
>
> No 1-9 or 1-10 PTH fragment is disclosed. The disclosure is on 1-8 PTH fragment. (The Final Office Action at pages 3-4.)

The Examiner further responded to the applicants' submission of Mr. Cantor's declaration (3/23/2007), Rebuttal Expert Report of Richard A. Lerner, M.D. (Lerner Report) and applicants' arguments on the written description/new matter issue. (The Final Office Action at pages 4-7.)

The presently pending claims have been amended and do not recite "an antibody binds to a bioactive epitope of a parathyroid hormone (PTH) in PTH_{1-8} or PTH_{1-9} wherein said isolated antibody binds to said epitope within a whole PTH with a higher affinity than its binding to said epitope within a PTH fragment selected from a PTH_{1-8} fragment, PTH_{1-9}, PTH_{1-10} and PTH_{1-34} fragment," The written description/new matter issue is rendered moot by the present amendments. In addition, as discussed below, the presently pending find support in the present application and in the parent applications.

The presently pending claims are directed to isolated antibody or isolated polyclonal antibody that specifically binds to a three-dimensional epitope of a parathyroid hormone (PTH) in PTH_{1-8} as part of whole PTH, wherein at least four amino acids in PTH_{1-8} are part of the reactive portion of said isolated antibody.

The present application claims priority and incorporates by reference the teachings of the parent application, the '422 application. (The present application at page 1, lines 20-22, and page 20, lines 13-14.) The '422 application teaches:

> To create an affinity-purified anti-(1-8) PTH antibody, one first uses a selected initial PTH sequence peptide as described above as part of an immunogen for injection into a goat. The peptide can be used either by itself as an injectible immunogen, incorporated into a non PTH peptide having a molecular weight, typically, of between about 5000 and 10,000,000, or as part of the wPTH complete sequence. (The '422 application at page 8, lines 24-28, emphasis added.)

Accordingly, the present application, via incorporating by reference the teachings of the '422 application, teaches generating an anti-PTH antibody by immunization with the "wPTH complete sequence." The '422 application also teaches:

> In order to make the signal antibody in the above assay, first one makes a synthetic PTH peptide corresponding either to hPTH (Ser-Val-Ser-Glu-lie-Gln-Leu-Met), SEQ ID NO:4, rat PTH (Ala-Val-Ser-Glu-lie-Gln-Leu-Met), SEQ ID NO:5, or at least four amino acids in the common sequence, absent the first amino acid. The selected peptide can play two roles in making an assay, first as a specific antigenic source for creating a polyclonal antibody or monoclonal antibody source for signal antibody or capture antibody, and second as part of an affinity purification means for isolating the desired signal antibody or capture antibody. (The '422 application at page 7, line 26 through page 8, line 2, emphases added.)

Therefore, the present application, via incorporating by reference the teachings of the '422 application, teaches affinity purification of an anti-PTH antibody, from antisera generated by immunization with the "wPTH complete sequence," using human PTH_{1-8} sequence, rat PTH_{1-8}

sequence, or at least four amino acids in the common sequence. In other words, the present application teaches antibodies that specifically bind to an epitope in PTH_{1-8} as part of whole PTH.

In addition, the present application teaches "a first antibody or antibody fragment specific for the PTH peptide SER-VAL-SER-GLU-ILE-GLN-LEU-MET (SEQ ID No. 4), wherein at least four amino acids are part of the antibody reactive portion of the peptide." (The present application at page 5, lines 27-30; *see also* the '639 application at page 5, lines 26-29.) Accordingly, the present application teaches antibodies that specifically bind to an epitope in PTH_{1-8} as part of whole PTH and at least four amino acids in PTH_{1-8} are part of the reactive portion of the isolated antibodies.

The present application further teaches "[i]n making a measurement of wPTH, one does not want to detect PIN." (The present application at page 5, line 25; *see also* the '639 application at page 5, line 24.) The present application further teaches "PIN" is "a large, non-whole PTH peptide fragment." (The present application at page 5, lines 12-15; *see also* the '639 application at page 5, lines 11-14.) Accordingly, the present application further teaches an isolated antibody that does not specifically bind to a non-(1-84) PTH fragment.

The only limitation that the present application does not explicitly teach is that the isolated antibody specifically binds to a three-dimensional epitope in PTH_{1-8} as part of whole PTH. However, as discussed above, the present application does teach isolated antibodies that specifically bind to an epitope in PTH_{1-8} as part of whole PTH, and at least four amino acids in PTH_{1-8} are part of the reactive portion of the isolated antibodies. It is known in the art that PTH_{1-8} as part of whole PTH contains three dimensional structures or conformations. For example, Fiskin et al., *J. Biol. Chem.*, 252(22):8261-8 (1977) (Exhibit A) analyzed images of parathormone obtained by dark field electron microscopy in order to determine the three-dimensional structure of the molecule. Based on their analysis, Fiskin et al. postulated a model for the PTH three dimensional structure or conformation. (*See* Figure 6 of Fiskin at page 8267, and page 8265, right col.) As shown in the model depicted in Figure 6, the PTH (1-8) amino acid residues as part of whole PTH form an α-helix three dimensional structure or conformation.

Further, it is known in the art that there are 3.6 amino acid residues per turn of α helix:

> The α helix is a rodlike structure. The tightly coiled polypeptide main chain forms the inner part of the rod, and the side chains extend outward in a helical array (Figures 2-31 and 2-32). The α helix is stabilized by hydrogen bonds between the NH and CO groups of the main chain. The CO group of each amino acid is hydrogen bonded to the NH group of the amino acid that is situated four residues ahead in the linear sequence (Figures 2-33). Thus, all the main-chain CO and NH groups are hydrogen bonded. Each residue is related to the next one by a translation of 1.5 Å along the helix and a rotation of 100°, which gives 3.6 amino acid residues per turn of helix. Thus, amino acids spaced three and four apart in the linear sequence are spatially quite close to one another in an α helix. In contrast, amino acids two apart in the linear sequence are situated on opposite sides of the helix and so are unlikely to make contact. The pitch of the α helix is 5.4 Å, the product of the translation (1.5 Å) and the number of residues per turn (3.6). (Exhibit B., Stryer, at pages 26-27; emphases added.)

Accordingly, if an antibody binds to at least four amino acid residues in PTH_{1-8} as part of whole PTH, due to the three dimensional structure contained in PTH_{1-8} as part of whole PTH, the antibody necessarily binds to sufficient number of amino acid residues that form part of the three dimensional structure, *i.e.*, the antibody necessarily binds to a three-dimensional epitope in PTH_{1-8} as part of whole PTH.

Therefore, given that the present application teaches antibodies that specifically bind to an epitope in PTH_{1-8} as part of whole PTH, and at least four amino acids in PTH_{1-8} are part of the reactive portion of the isolated antibody, and given that PTH_{1-8} as part of whole PTH necessarily contains a three dimensional structure, and binding to at least four amino acids in PTH_{1-8} as part of whole PTH necessarily binds to a three-dimensional epitope in PTH_{1-8} as part of whole PTH, it follows that the present application, at least inherently, teaches isolated antibodies that specifically bind to a three-dimensional epitope in PTH_{1-8} as part of whole PTH, and the present amendments do not introduce any new matter. *See* MPEP § 2163.07(a), citing *In re Reynolds*, 443 F.2d 384, 170 USPQ 94 (CCPA 1971); *In re Smythe*, 480 F. 2d 1376, 178 USPQ 279 (CCPA 1973) (By disclosing in a patent application a device that inherently performs a function or has a property, operates

according to a theory or has an advantage, a patent application necessarily discloses that function, theory or advantage, even though it says nothing explicit concerning it. The application may later be amended to recite the function, theory or advantage without introducing prohibited new matter.). In addition, because the parent applications have the same or similar disclosures, the presently amended claims are entitled to the filing dates of the parent applications.

In view of the foregoing, applicants respectfully request reconsideration and withdrawal of this lack of written description/new matter rejection of the presently pending claims.

CONCLUSION

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the event the U.S. Patent and Trademark office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to Deposit Account No. 03-1952 referencing docket no. 53221200624. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Dated: November 5, 2009

Respectfully submitted,

Electronic signature: /Peng Chen/
Peng Chen
Registration No.: 43,543
MORRISON & FOERSTER LLP
12531 High Bluff Drive, Suite 100
San Diego, California 92130-2040
(858) 720-5117